



Year: 2017

A pilot randomized trial of exercise as adjunct therapy in a heroin-assisted treatment setting

Colledge, Flora ; Vogel, Marc ; Dürsteler-Macfarland, Kenneth ; Strom, Jonas ; Schoen, Susanne ; Pühse, Uwe ; Gerber, Markus

Abstract: Background: Although the potential of exercise as an adjunct treatment for substance dependence is persuasive in theory, few controlled trials have assessed its effectiveness. Existing research has also largely focused on individuals aiming towards, or having already achieved, abstinence. This study employed a randomized design in a pilot trial to assess the feasibility, acceptance, and effects of an exercise intervention for individuals receiving outpatient heroin-assisted treatment. Method: 50 individuals receiving heroin-assisted treatment at a clinic in Switzerland were invited to take part in the trial. Participants were randomized to 12 weeks of exercise twice per week, or a corresponding duration of non-exercise group activities in a comparison condition. Data on attendance, compliance, and numerous psychological and physiological parameters were gathered. Results: 24 individuals were willing to take part in the study. 92.3% of the exercise condition ($n = 13$) were compliant or semi-compliant with the protocol; by contrast, only 54.6% of participants in the comparison condition ($n = 11$) were compliant or semi-compliant ($\chi^2 = 7.049$; $p = 0.029$). Participants in the exercise condition significantly increased the number of minutes spent exercising at a high intensity level ($F(2,44) = 3.794$; $p = 0.046$; $\eta^2 = 0.159$). No other significant interaction effects were observed. Conclusions: An exercise intervention is a feasible and accepted supplementary therapy to heroin-assisted treatment. Participation rates were high, particularly given the outpatient setting. No evidence regarding the potential mechanisms of exercise as a therapy modality could be identified. Patients in heroin-assisted treatment may require a longer-term exercise programme, specifically targeting particular health parameters, before measurable improvements can be observed.

DOI: <https://doi.org/10.1016/j.jsat.2017.01.012>

Posted at the Zurich Open Repository and Archive, University of Zurich

ZORA URL: <https://doi.org/10.5167/uzh-148419>

Journal Article

Accepted Version



The following work is licensed under a Creative Commons: Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0) License.

Originally published at:

Colledge, Flora; Vogel, Marc; Dürsteler-Macfarland, Kenneth; Strom, Jonas; Schoen, Susanne; Pühse, Uwe; Gerber, Markus (2017). A pilot randomized trial of exercise as adjunct therapy in a heroin-assisted

treatment setting. *Journal of Substance Abuse Treatment*, 76:49-57.
DOI: <https://doi.org/10.1016/j.jsat.2017.01.012>

A pilot randomized trial of exercise as adjunct therapy in a heroin-assisted treatment setting

Flora Colledge^a, Marc Vogel^b, Kenneth Dürsteler-Macfarland^b, Jonas Strom^b, Susanne Schoen^b, Uwe Pühse^a, Markus Gerber^a.

a Department of Sport, Exercise and Health, University of Basel, Birsstrasse 320b, 4052, Basel, Switzerland

b University Psychiatric Clinics, University of Basel, Wilhelm Klein-Strasse 27, 4012, Basel, Switzerland

Corresponding Author:

Flora Colledge

Department of Sport, Exercise and Health, University of Basel, Birsstrasse 320b, 4052, Basel, Switzerland

Email: flora.colledge@unibas.ch

Tel: +41 61 3778787

Background

Although the potential of exercise as an adjunct treatment for substance dependence is persuasive in theory, few controlled trials have assessed its effectiveness. Existing research has also largely focussed on individuals aiming towards, or having already achieved, abstinence. This study employed a randomised controlled design in a pilot trial to assess the feasibility, acceptance, and effects of an exercise intervention for individuals receiving outpatient heroin-assisted treatment.

Method

50 individuals receiving heroin-assisted treatment at a clinic in Switzerland were invited to take part in the trial. Participants were randomised to 12 weeks of exercise twice per week, or a corresponding duration of non-exercise group activities in a comparison condition. Data on attendance, compliance, and numerous psychological and physiological parameters were gathered.

Results

24 individuals were willing to take part in the study. 92.3% of the exercise condition (n=13) were compliant or semi-compliant with the protocol; by contrast, only 54.6% of participants in the comparison condition (n=11) were compliant or semi-compliant ($\chi^2=7.049$; $p=.029$). Participants in the exercise condition significantly increased the number of minutes spent exercising at a high intensity level ($F(2,44)=3.794$; $p=.046$; $\eta^2=.159$). No other significant interaction effects were observed.

Conclusions

An exercise intervention is a feasible and accepted supplementary therapy to heroin-assisted treatment. Participation rates were high, particularly given the outpatient setting. No evidence regarding the potential mechanisms of exercise as a therapy modality could be identified. Patients in heroin-assisted treatment may require a longer-term exercise programme, specifically targeting particular health parameters, before measurable improvements can be observed.

Keywords

Heroin; opiates; heroin-assisted treatment; exercise; treatment

1. Introduction

The recognition that exercise is a fundamental aspect of good human health, which may not only prevent many diseases, but also be therapeutically effective, has grown rapidly in the last two decades. Numerous studies have reported the positive influence of an exercise regimen for a range of illnesses, especially cardiovascular and metabolic diseases (Pattyn, Cornelissen, Eshghi, & Vanhees, 2013; Taylor et al., 2004). In particular, there has been an increased interest in the potential of exercise as an adjunct treatment for mental disorders (Richardson et al., 2005; Rosenbaum, Tiedemann, Sherrington, Curtis, & Ward, 2014). The strongest evidence exists for the treatment of depression (Blumenthal et al., 2007; Cooney et al., 2013), with certain beneficial effects for anxiety disorders and schizophrenia (Callaghan, 2004), although evidence from methodologically robust studies is sparse, and frequently less promising than from studies without control conditions (Zschucke, Gaudlitz, & Ströhle, 2013).

Substance dependence is a mental disorder frequently accompanied by comorbidities such as depression, anxiety disorders and personality disorders (Volkow, 2001). It is treated with pharmaceutical and therapeutic modalities (in some cases encompassing a withdrawal period) in ways similar to those employed for other mental disorders (Kleber et al., 2006). To date, studies assessing the potential of exercise as an adjunct treatment for substance use disorders have varied considerably in primary outcomes, and in quality.

Evidence from preclinical studies suggests that, with the exception of alcohol, undertaking exercise reduces drug self-administration, escalation, and reinstatement. A number of mechanisms have been posited, most importantly the rewarding properties of exercise due to activation of the mesolimbic pathway, the amelioration of striatal dopamine receptor deficits (Robertson et al., 2015), and the concurrent reduction of comorbidities which may perpetuate the substance use cycle (Lynch et al., 2013). Some authors have speculated that the caloric content of alcohol, and the route of administration may account for the inconsistency of studies involving ethanol (Bardo & Compton,

2015; Lynch, Peterson, Sanchez, Abel, & Smith, 2013). Though purely speculative, we suggest that dopamine release and, possibly, receptor availability, following alcohol administration may differ from other substances to a degree which may also contribute to the findings summarised above (Nutt, Lingford-Hughes, Erritzoe & Stokes, 2015).

Evidence from clinical trials, although promising, remains in the early stages. A recent literature review reports on eight studies examining exercise as an adjunct treatment for substance use, which showed weak evidence for positive effects on a variety of outcome variables (Zschucke, Heinz, & Ströhle, 2012) such as increases in days of abstinence (Brown et al., 2010; Burling, Seidner, Robbins-Sisco, Krinsky, & Hanser, 1992; Collingwood, Reynolds, Kohl, Smith, & Sloan, 1991), decreased heroin withdrawal symptoms (Li, Chen, & Mo, 2002), and reduced craving (Buchowski et al., 2011; Roessler, 2010). The review also speculates that in clinical populations, numerous social, behavioural and neurophysiological mechanisms may be implicated in the effects of exercise interventions, although no study has examined these in detail. A wide variety of exercise forms, including strength training, Qi Gong, aerobic training using circuits, exercise bikes and treadmills, softball games, volleyball, and in some cases a number of these combined, have been employed with frequencies varying from one to five times per week.

Since that review, a pilot randomized controlled trial with 29 individuals currently receiving methadone treatment has demonstrated that a video-game based intervention, involving 25 minutes of a combination of aerobic training, strength training, and flexibility exercises undertaken individually, is a feasible and acceptable method of exercise participation for this population. Participants also significantly reduced their cocaine and opioid use, and experienced improved mental wellbeing, although there was no difference between the exercise or control group (Cutter et al., 2014). In a study by Dolezal (2013) and colleagues, 39 individuals following inpatient treatment for methamphetamine dependence were randomized to an exercise intervention involving three hour-long sessions of treadmill running and strength circuits, or a control condition. As well as showing the feasibility of the intervention, the exercise group significantly improved VO₂max (the

maximum volume of oxygen that an individual can use during exercise)(Hawkins, Raven, Snell, Stray-Gundersen, & Levine, 2007) and muscle strength (Dolezal et al., 2013). In a subsequent study in this population, with the same exercise protocol, heart rate variability improved following eight weeks of training (Dolezal et al., 2014).

Although not a clinical trial, Weiss and colleagues report, based on interviews with recovered or relapsed heroin addicts, that participating in exercise, amongst other activities, can be helpful in achieving abstinence (Weiss et al., 2014). Further research is also currently in development; Mooney (2014) and colleagues are developing an aerobic and resistance training programme, to be supervised thrice weekly over an 8-week period following residential treatment for methamphetamine dependence, while Trivedi (2011) and colleagues have designed a 12 week programme of thrice weekly treadmill-training, followed by 6 months of once-weekly supervised sessions for individuals undertaking residential treatment for stimulant abuse. Both studies focus on days of abstinence following residential care as the primary outcome (Mooney et al., 2014; Trivedi et al., 2011).

While these studies have shown tentatively promising results, Zschucke (2012) and colleagues note that many have been plagued by issues, such as small sample sizes and high drop-out rates, which limit their statistical power (Zschucke, Heinz & Ströhle, 2012). Furthermore, to date, all but one of the studies have been carried out with individuals already abstinent and not receiving opioid substitution therapy, and aiming towards long-term abstinence. It remains to be seen whether an exercise programme is feasible, acceptable and effective for individuals for whom abstinence is not a current realistic possibility, and who are not in a setting (such as inpatient care), in which regular structured exercise can be relatively easily carried out.

In Switzerland, and a small number of other countries, heroin-assisted treatment (HAT) is offered for opioid-addicted individuals who have failed to respond to conventional treatment, such as methadone substitution or abstinence-oriented treatment (Bundesamt für Gesundheit, 2015).

Patients are prescribed a dose of clinical-standard heroin (diacetylmorphine), which they inject or ingest within the clinic once or twice per day. The principal aim of HAT is to provide patients with a treatment modality which will enable them to stabilise their lives, and avoid the illegal behaviour which opioid consumption otherwise necessitates (Bundesamt für Gesundheit, 2000). A review of studies of HAT in Canada, Switzerland, Germany, the Netherlands, and the United Kingdom, found the treatment to be safe, effective in reducing delinquent behaviour and illicit opioid consumption, and a valuable, if “last-resort” treatment option (Fischer et al., 2007). The Swiss Department of Health lists overall health, and specifically exercise promotion amongst the mid-term aims of HAT (Bundesamt für Gesundheit, 2000). To date, however, the feasibility of integrating an exercise programme into this treatment form has not been investigated.

The aim of the present randomised pilot study was to test the feasibility, acceptability and psychological and physiological health effects of an exercise programme in an out-patient HAT setting, for opioid-addicted individuals not aiming towards abstinence at the time of the study. In order to minimise the potential confounding effects of the intervention being associated with contact time with new team leaders, access to typically prohibitively expensive environments, and a financial reward, a comparison condition was used in this study. In this way, it is hoped that patient attitudes to sport specifically can be disentangled from patient attitudes to new activities and study participation in general. In contrast with the majority of other studies in this field, in which abstinence was a central outcome, relevant outcomes for individuals in HAT should be seen as potential harm reduction measures, such as reduced illicit drug consumption. Four research questions were formulated in line with this aim:

- 1.1 Can HAT patients be recruited to participate in an RCT of exercise as an adjunct treatment modality?
- 1.2 Will the exercise group comply with the study protocol?
- 1.3 Will the comparison group comply with the study protocol?

1.4 Will an exercise programme lead to any alterations or improvements in the above-mentioned variables, and will these differences also be found in the comparison group?

2. Methods

The study took place between November and February 2014, and was part of larger study into exercise as feasible treatment in outpatient opiate substitution therapy.

2.1 Participants and procedures

Participants were recruited from a HAT clinic, treating 150 patients, in Basel, Switzerland.

Participants were recruited via face-to-face contact with study or clinic personnel, and informative posters and flyers in the clinic. The sole exclusion criterion was any psychological or physical impairment precluding participation in light exercise, a decision made solely by the treatment staff of the clinic. In total, 50 patients were deemed capable of taking part, and were invited to join the study. Patients who agreed to participate were randomised to either an exercise or comparison condition through a blinded process of identical sealed envelopes, stipulating one of the two conditions. Patients were informed verbally and in writing that, if they were in the comparison group, they would also receive 12 weeks of exercise training immediately upon completion of the study. All patients were informed that in addition to drinks and snacks following training, they would receive a sports T-shirt, and 100 Swiss francs as reward for participation. Patients were informed that if they missed more than five training sessions, this reward would be reduced by four francs for each session missed, although even non-compliance with the protocol resulted in a small reward for completion of the study measures. All patients provided written informed consent. The study was carried out in accordance with the principles of the Declaration of Helsinki, and approval for the trial was obtained from the local ethics committee (EKNZ), an independent organisation representing 11 Swiss cantons.

It is important to note that there is no penalty for use of additional substances in HAT in Switzerland, so this would not constitute a reason for reticence in answering questions regarding concomitant

substance use. The consumption of other substances was assessed as one of the outcomes of this study, as is described further below.

2.2 Intervention programme

The exercise condition was designed with regard to feedback received from patients during preliminary qualitative investigations. Questionnaires and focus groups were used to determine the optimal organisation, content and timing of the programme. Specifically, the questionnaire (N=28) revealed that clinic patients were keen to become more physically active, but had a wide variety of exercise preferences which frequently overlapped with those activities which other patients refused to participate in. The focus group (N=12) was used to determine the optimal days and times for the intervention to take place, the importance of location and material provision, and to determine an intervention structure which would allow all patients, regardless of physical ability, to participate. (Detailed information on these findings appears in a forthcoming publication). In order to provide appealing content for all ability levels, two parallel exercise sessions were offered on two evenings per week, following dispensing of diacetylmorphine. One session involved moderate to vigorous physical activity which varied regularly in terms of content (including climbing, badminton, strength training, boxing, dance). The second session involved walking, occasionally with coordination games, to include participants with physical limitations or dislike of the other sport activities. Patients could decide freely at the start of every session which group they would prefer to join. No specific heart rate zone or energy expenditure goals were set for these sessions. Based on patient feedback, it was determined that in the pilot phase of research, participation as such, and not the achievement of fitness targets, was the appropriate aim for this population. The sessions, and the comparison group activities, were overseen by four trained study personnel with a background in sports education.

The comparison condition was scheduled at the same time and with the same frequency, but without a parallel session, as physical impairments did not affect the comparison group activities in the same way as they might hinder participation in sports activities. Initially planned activities included board

games and painting; at the request of participants, cooking, museum visits and billiard games were also included. While some of these activities do include a certain amount of physical movement, as they are not “planned, structured and repetitive” (Caspersen, Powell & Christenson, 1985) in the manner of exercise training, we feel that their incorporation into the comparison condition does risk obscuring any effects of the exercise condition.

Neither group received advice to change their exercise or substance consumption habits, or were given any other form of health advice in the context of the study.

2.3 Measures

Data was collected at baseline following randomisation, after 6 weeks, and at the end of the 12 week programme. Measurements took place in the clinic during morning and afternoon opening hours. All demographic and psychological questionnaires were completed with pen and paper by participants, with study personnel guidance. Physiological measures were taken by study personnel and entered into the paper case report form immediately. The measures employed in this study were chosen primarily on the basis of their validity and reliability in assessing the relevant constructs, with consideration given to whether the original questionnaire was in German. However, a particular focus was also placed on brevity, as the full questionnaire booklet comprised 13 (one-sided) pages, and it was judged that a lengthier booklet might pose an additional hurdle for participants. All measures used were also employed in the subsequent stages of this study carried out in a further opioid substitution clinic.

Demographic data concerning age, gender, nationality, highest education level achieved, employment/social support status and marital status were reported by each participant. We also assessed the daily dose of diacetylmorphine and clinical diagnoses of psychiatric comorbidities from the electronic patient file.

Compliance with the study protocol was categorised as follows: compliant (at least 18 out of 23 sessions attended); semi-compliant (between 17 and 5 sessions attended); and non-compliant (4

sessions or fewer attended). Compliance and non-compliance were defined as approximating 80% (or more) and 20% (or less) attendance respectively. The broad semi-compliance category was deemed the best way to represent the irregular attendance displayed by certain participants. Furthermore, as participants were informed prior to the study that missing more than 5 sessions, or attending 4 or fewer, would impact on the financial reward they received, it was felt that this categorisation reflected the expectations explicitly communicated to participants in the study, and was therefore an appropriate approach.

2.4 Psychological measures

Depressive symptoms were assessed with the German version of the Centre for Epidemiologic Studies Depression Scale (Allgemeine Depressionskala – Kurz), a 15 item self-report measure of depressive mood, which respondents scored on a 4-point Likert-type scale from 0 (never or very rarely) to 3 (always or nearly all the time) (Hautzinger & Bailer, 1993). A clinical cut-off score of 18 or above, with high specificity and sensitivity, indicates the presence of a depressive state. The Depression Scale is a widely used, quick instrument, and reliability and validity data have been documented for use within general and clinical populations (Lehr, Hillert, Schmitz, & Sosnowsky, 2008).

Subjective sleep was assessed using the self-report Insomnia Severity Index (ISI) (Bastien, Vallières, & Morin, 2001). The ISI aims to detect subthreshold (score of 8-14), mild (score of 15-21), and severe (score of 21-28) insomnia. Participants respond to seven questions on a 5-point Likert-type scale ranging from 0 (e.g., not at all) to 4 (e.g., very severe) concerning sleep quality, and impact and severity of any disturbances in the previous two weeks. The scale has excellent internal consistency and good convergent validity (Morin, Belleville, Belanger, & Ivers, 2011).

Self-control was assessed using the Brief Self Control Scale (BSCS) (Maloney, Grawitch, & Barber, 2012). The scale comprises 13 items measured on a 5-point Likert-type scale, with answers varying from 1 (not true) to 5 (completely true). This measure evaluates the responder's tendency towards

traits and habits associated with high self-control. The BSCS has good internal consistency and retest reliability (Tangney, Baumeister, & Boone, 2004).

The Perceived Stress Scale (PSS) (Cohen, Kamarck, & Mermelstein, 1983) was used to measure the degree to which respondents report various aspects of their life as stressful. Responses are given on a 5-point Likert scale ranging from 1 (never) to 5 (very often). The PSS has good reliability and validity (Roberti, Harrington, & Storch, 2006).

The 36-item short-form health survey questionnaire (SF-36) encompasses eight multi-item dimensions of health (physical functioning, social functioning, physical problems, emotional problems, mental health, vitality, pain, and general health perception) (Brazier et al., 1992). The German version of the SF-36 shows good reliability and construct validity (Bullinger, 2000).

2.5 Substance use

Substance use was measured using the Timeline Follow-back (TLFB) questionnaire (Sobell & Sobell, 1996). This calendar system, administered by an investigator, is used as a tool to help participants recall their consumption of substances, and the amount consumed, for the past 30 days. In the present study, specified substances were: cigarettes; alcohol; illicit medication; street heroin; cocaine; and other illicit substances such as marijuana and LSD. The total number of days on which any substances, excluding cigarettes and alcohol, were consumed, was also calculated. The TLFB has excellent reliability and validity (Hjorthøj, Hjorthøj, & Nordentoft, 2012; Sobell, Maisto, Sobell, & Cooper, 1979).

2.6 Self-reported activity

The International Physical Activity Questionnaire Short Form (IPAQ-SF) was used to assess the physical activity levels of participants over the previous seven days. This simple measure comprises six questions concerning the number of days, and minutes per day, on which respondents were vigorously, moderately and lightly physically active, respectively. The IPAQ-SF is easy and quick to

administer and has satisfactory validity (Craig et al., 2003; van Poppel, Chinapaw, Mekkink, van Mechelen, & Terwee, 2010). While it has been shown that the IPAQ-SF can lead to an overestimation of activity, its usefulness in repeated measures studies remains accepted, and the ease of use and internationally standardised versions make it an appropriate measure for the current study (Lee, Macfarlane, Lam, & Stewart, 2011).

2.7 Physiological measures

Blood pressure was taken using a digital sphygmamometer, following the protocol described by Pickering and colleagues (Pickering et al., 2005). Patients were seated, instructed to avoid speech and movement, and the measurement was carried out by study personnel. Three measures were taken, each separated by a minute, and the mean value was calculated for analysis.

Hand grip strength was measured using a SH 5001 Hydraulic Hand Dynamometer (Saehan Corporation) calibrated by the manufacturer. Participants performed the test seated, following the detailed protocol described by Bellace (2000) and colleagues (Bellace, Healy, Besser, Byron, & Hohman, 2000). Three measurements for each hand were taken, alternating after each effort and rest period, and the mean value was calculated for analysis.

The handgrip strength test represents a physiological measure which has been shown to predict the development of future health complications and premature mortality (Sasaki et al, 2007). Although in a study examining the effects of exercise, a more direct assessment of fitness change, such as VO2 Max testing, is highly desirable, the difficulty of performing multiple laboratory tests with each participant, and the physical complaints experienced by some when walking briskly, rendered such testing unfeasible.

2.8 Statistical analysis

Demographic data was analysed using one-way univariate analysis of variance (ANOVA) and Chi-squared tests. Physiological and psychological variables were analysed using repeated measures

ANOVAS, with the independent factors of Group (exercise vs. comparison) and Time (baseline, 6 weeks, 12 weeks). Where Mauchly's test of sphericity was significant, the Greenhouse-Geisser correction was applied. For all analyses, the level of significance was set at $p \leq 0.05$. Cohen's ω effect sizes for the Chi-squared tests and ANOVAS were interpreted as follows: >0.1 , small; >0.3 , medium; >0.5 , large; and >0.01 , small; >0.06 , medium; >0.14 , large, respectively (Cohen, 1977). Statistical analysis was performed using SPSS 21 (IBM Corporation, Armonk NY, USA) for Windows. An intention-to-treat analysis was not employed as, while a number of participants missed varying numbers of sessions, all participants completed the measures employed over the three measurements points.

3. Results

Following invitation, 22 patients indicated that they did not wish to participate in the study. Reasons cited were inability to participate at the time in question ($n=4$), unwillingness to commit to 12 weeks of participation ($n=17$), and unwillingness to participate without a guarantee that they would end up in the exercise group ($n=1$). Following randomisation, three members assigned to the comparison group and one assigned to the exercise group withdrew consent for the study. The remaining 24 comprised 13 participants in the exercise group and 11 in the comparison group.

Sociodemographic data for both groups is given in Table 1. The exercise group did not differ significantly from the comparison group on any aspect. The mean age and gender distribution reflects the current means of the HAT population in Switzerland (Hiltebrand, Dickson-Spillmann, Bolliger, & Schaub, 2015).

Data on compliance with the study protocol and attendance per session can be found in Table 2 and Figure 1. There was a significant difference in compliance between the exercise and comparison groups. Members of the comparison group were more frequently non-compliant, and less frequently semi-compliant. The proportion of participants with high compliance was similar in both groups with 39% (exercise) and 46% (comparison).

Results of the psychological assessments are shown in Table 3. The exercise group scored significantly better than the comparison group across all time points including baseline on the first dimension of the SF-36, which reflects physical functioning. A large effect size was observed for this variable. A medium effect size for time by group was also observed for the second dimension of the SF-36, which reflects limitations in usual activities due to physical problems. A large effect size for group was observed for the seventh dimension of the SF-36, which reflects limitations in usual activities because of emotional problems. Aside from this, there were no significant effects of time, group, or time by group.

Findings for concomitant substance use are shown in Table 4. Medium effect sizes for time by group interaction were found for sum days of concomitant substance use, days of cigarette use, and days of illicit use of prescription drugs. There were no significant effects of time, group, or time by group.

Data for self-reported activity and physiological variables are shown in Table 5. A significant time by group interaction effect and large effect size was observed for the number of minutes per day of vigorous physical activity, although not for the number of days per week on which this exercise was performed. A large effect size for group was also observed for the number of minutes per day spent on foot. There were no further significant effects observed for self-reported activity. However, descriptively, the exercise group reported a decrease in minutes per day spent in moderate exercise.

The exercise group showed significantly greater right and left hand-grip strength, with large effect sizes for group, compared to the comparison group. Otherwise, there were no significant effects of time, group, or time by group on the physiological variables.

4. Discussion

The current study assessed the feasibility and acceptability of an exercise programme in a HAT setting, and further explored effects on a number of psychological, behavioural and physiological variables. Based on the findings, it can be concluded that an exercise intervention is both feasible and accepted in this setting. While no effects on psychological or physiological functioning were

observed, it is important to emphasise that an intervention with measurable effects, but which the target population does not want to take part in, is not a valuable addition to treatment. This study represents a first step towards further integration of exercise in outpatient substance dependence treatment settings, which it is hoped will lead to a broader evidence base regarding the effects of exercise.

Just under half of the patients invited to take part in the study participated. It can therefore be concluded that patients in this HAT clinic can be recruited to participate in an exercise programme. It must also be noted that HAT is an outpatient treatment, and the participation rates are all the more notable for the fact that patients took extra time out of their days to participate, rather than participating as a means to fill in time during inpatient treatment. However, it must also be noted that in a clinic of approximately 150 patients, 24 willing and able participants represents a rate of 16%. The voluntary nature of the study naturally means that mainly individuals already interested in exercise chose to participate; this level of bias is almost impossible to exclude in non-blinded research. This phenomenon may also partly be reflected in the significantly lower participation of the-comparison group. Accordingly, it must be noted that while compliance levels were promising, the acceptability of such an intervention must be interpreted in light of the fact that many patients in a clinic of this kind may not be suitable candidates for an exercise programme.

In the sole other study to examine the effects of exercise in patients receiving opioid substitution therapy, specifically methadone maintenance, it was concluded that active video-game play, an accepted form of physical exercise, was a feasible addition to treatment (Cutter et al, 2014). With 23% of all clinic patients participating in the study, acceptability of this intervention can be deemed slightly higher, though not dissimilar, to our study. Interestingly, the comparison group in Cutter's (2014) study, playing sedentary video games, appeared to be equally compliant with the study protocol compared to the exercise game players. It may be that video-games are a most promising comparison condition for research with this population. However, while decreases in secondary substance consumption and stress were reported in this study, there was no difference between

groups. While this very limited literature does not foster confident conclusions, it would appear that patients in opioid substitution treatment are willing to engage in exercise, and enjoy it, but the anticipated improvements in well-being are not measurable over time spans of a few months. Individuals in this form of treatment have, in the majority of cases, been substance dependent for a number of years, and consequently may require long term interventions to show any changes in physical or psychological status. Although challenging to engage in, studies which assess effects of such programmes over many months may provide evidence of measurable effects.

Only 54.6% of comparison group members were compliant or semi-compliant with the study protocol, in spite of the fact that they were frequently reminded that they would receive 12 weeks of exercise training following the study period if they desired, and it was emphasised that this offer was not conditional upon attendance at a certain number of comparison meetings; equally, participation in this subsequent offer was not required, or associated with further analysis. On the one hand, this has the consequence that no further follow-up data is available; on the other, it was intended to ensure that participation in the comparison group was not negatively associated with the duty to commit to 24, rather than 12, weeks of research. Our finding suggests that a randomized study design may be complicated to implement in this population. Full blinding is impossible in such interventions, and the choice between a controlled trial, or a comparison trial, can impact on the study outcomes, and must therefore be guided by them. As outlined above, our rationale for including a comparison group which took part in outings with the study personnel was to minimise the potential confounding effects of contact time, access to special locations, and financial reward. Had the comparison group received only treatment as usual, any positive development observed in the exercise group would be questionable. A wait-list control condition represents a potential solution to this situation; however, our experience suggested that even this approach may cause problems for participant retention, as a number of individuals in this study refused to participate if it could not be guaranteed that they could begin exercise immediately, rather than in 12 weeks. Further, again as noted above, this doubles the commitment time for participants, a factor which

should not be underestimated during recruitment. An ITT analysis will be essential in such cases.

Based on our study design and findings, we feel we can cautiously suggest that participating in exercise itself, and not just a somewhat lucrative study, may be judged to be attractive for HAT patients; subsequent studies may produce more significant results if they are able to combine successful recruitment with a randomized controlled design.

In line with research questions 1.1, 1.2, and 1.3, it appears therefore appears that HAT participants can be recruited to such a study, and that compliance with the exercise protocol significantly exceeded compliance with the ~~control~~ comparison condition.

The present study implemented patient feedback to design the exercise programme, thus enabling patients to determine the type and intensity of activity they participated in. In addition to demonstrating respect for patient's wishes, there is evidence that self-paced exercise results in more positive affective response than prescribed intensity exercise (Williams, 2008); this may be an important factor in maintaining adherence rates in this population.

Although this approach may have had a favourable impact on participation rates, the decision to forgo testing of fitness parameters and training effects means that data regarding the physiological impact of the chosen methodology is not available; this holds true even when the data for handgrip strength are assessed. While handgrip strength has been associated with a number of health outcomes, as outlined in the Methods section, in this study there were no significant changes over time. Despite the ease of testing handgrip strength, we acknowledge that this distal marker of health outcomes may be less reactive to a fitness intervention than VO2 Max testing, for example, which may be the next step for research in this setting.

While it is difficult to speculate on the success of a longer-term exercise programme, we suggest that the regular participation of the sport group (as compared to the control group) in this study, and, importantly, the clinic structure in the HAT setting (daily patient contact, patient interaction) are key factors which may be positive indicators of long-term adherence. Indeed, it is possible that a longer

term programme may lead to an increase in participation, as individuals initially unwilling to participate may be more likely to trust and accept an established programme recommended by peers.

In line with the compliance of the exercise group with the study protocol, this group reported a significant increase in minutes per day spent in vigorous physical activities at the end of the study period. Consequently, it can be concluded that the increase in activity was received as such, and reliably reported, by this group. Participation in physical activity, especially vigorous physical activity, has a positive effect on all-cause mortality (Gebel et al., 2015; Hupin et al., 2015). Interestingly, the exercise group also reported a descriptively, but not significantly reduced level of minutes per day spent moderately exercising at the end of the study. It may be that this group perceived their participation in the programme to be strenuous, and therefore reduced other activities in order to rest and recover for the “official” exercise programme.

There were no statistically significant effects observed for any of the other variables measured; research question 1.4 cannot be answered further. No data regarding the existence or effectiveness of hypothesised mechanisms of exercise as an adjunct treatment can be provided by this study. Improvements in these domains have been reported in other populations with mental disorders; it may be that changes would become significant with a larger sample, over a longer period of time, or with a structured training protocol, in the latter case especially where physiological changes are concerned.

Future directions

While the prevalence of opioid addiction has decreased in Switzerland and other European countries, the United States has recently experienced a resurgence, as the increase in opioid medication prescription has translated to increased rates of death associated with heroin (Dart et al., 2015). The results of this study are that exercise is a feasible, acceptable and desirable addition to HAT, but that standardised tests and questionnaires detect no significant improvements in a number of physical

and psychological parameters. The exercise intervention implemented here did not adhere to any specific intensity guidelines. Consequently, the next step in examining exercise as a potential adjunct treatment is to investigate whether one or several strict exercise protocols would result in measurable improvements in these or other parameters. As suggested by Linke and Ussher (2015) explicit development of exercise as a tool to cope with difficult situations and improve psychological health should also be tested.

Limitations

The present study has a number of limitations. First, as a pilot study, sample size may have been too small to detect some intervention effects. Second, the decision was made to allow patients to freely select the type and intensity of activity they participated in; hence, no associations between specific forms of exercise bout and the results presented here can be made. Self-report of physical activity, as noted above, may be unreliable, and future full scale studies may manage this issue by using objective physical activity trackers or cardiorespiratory fitness tests. Baseline differences were not included as covariates in the statistical analysis: While this renders the interpretation of treatment effects less clear, this approach was chosen to reflect the assessment of repeated measurements following the initial assessment. Finally, the decision to categorise individuals who attended between 17 and 5 sessions as “semi-compliant” means that a broad range of attendance was represented in this category, which could distort the findings. While it was felt that in this case, breaking the already small sample into further groups would be equally problematic, future studies may seek to pre-define more specific categories to permit a more detailed analysis.

Conflict of interest

None

Funding

This work was supported by Infodrog (Impulse and Development Fund for Addiction Research) [grant number 5025/14/BS/Substitution-Sport]

References

- Bardo, M. T., & Compton, W. M. (2015). Does physical activity protect against drug abuse vulnerability? *Drug and Alcohol Dependence*, 153, 3-13. doi: <http://dx.doi.org/10.1016/j.drugalcdep.2015.05.037>
- Bastien, C. H., Vallières, A., & Morin, C. M. (2001). Validation of the Insomnia Severity Index as an outcome measure for insomnia research. *Sleep Medicine*, 2(4), 297-307. doi: [http://dx.doi.org/10.1016/S1389-9457\(00\)00065-4](http://dx.doi.org/10.1016/S1389-9457(00)00065-4)
- Bellace, J. V., Healy, D., Besser, M. P., Byron, T., & Hohman, L. (2000). Validity of the Dexter Evaluation System's Jamar Dynamometer Attachment for Assessment of Hand Grip Strength in a Normal Population. *Journal of Hand Therapy*, 13(1), 46-51. doi: [http://dx.doi.org/10.1016/S0894-1130\(00\)80052-6](http://dx.doi.org/10.1016/S0894-1130(00)80052-6)
- Blumenthal, J. A., Babyak, M. A., Doraiswamy, P. M., Watkins, L., Hoffman, B. M., Barbour, K. A., Herman, S., Craighead W. E., Brosse, A.L., Waugh, R., Hinderliter, A., Sherwood, A. (2007). Exercise and pharmacotherapy in the treatment of major depressive disorder. *Psychosomatic Medicine*, 69(7), 587-596. doi: 10.1097/PSY.0b013e318148c19a
- Brazier, J. E., Harper, R., Jones, N. M., O'Cathain, A., Thomas, K. J., Usherwood, T., & Westlake, L. (1992). Validating the SF-36 health survey questionnaire: new outcome measure for primary care. *British Medical Journal*, 305(6846), 160-164.
- Brown, R. A., Abrantes, A. M., Read, J. P., Marcus, B. H., Jakicic, J., Strong, D. R., Oakley, J. R., Ramsey, S. E., Kahler, C.W., Stuart, G.G., Dubreuil, M.E., Gordon, A. A. (2010). A Pilot Study of Aerobic Exercise as an Adjunctive Treatment for Drug Dependence. *Mental Health and Physical Activity*, 3(1), 27-34. doi: 10.1016/j.mhpa.2010.03.001
- Buchowski, M. S., Meade, N. N., Charboneau, E., Park, S., Dietrich, M. S., Cowan, R. L., & Martin, P. R. (2011). Aerobic Exercise Training Reduces Cannabis Craving and Use in Non-Treatment

- Seeking Cannabis-Dependent Adults. *PLoS ONE*, 6(3), e17465. doi: 10.1371/journal.pone.0017465
- Bullinger, M. (2000). Erfassung der gesundheitsbezogenen Lebensqualität mit dem SF-36-Health Survey. [journal article]. *Bundesgesundheitsblatt - Gesundheitsforschung - Gesundheitsschutz*, 43(3), 190-197. doi: 10.1007/s001030050034
- Bundesamt für Gesundheit. (2000). *Handbuch Heroingestützte Behandlung. Richtlinien, Empfehlungen, Information*. Bern, Switzerland: Bundesamt für Gesundheit.
- Bundesamt für Gesundheit. (2015). *Handbuch Diacetylmorphingestützte Behandlung. Richtlinien und Erläuterungen zu den gesetzlichen Bestimmungen*. Bern, Switzerland: Bundesamt für Gesundheit.
- Burling, T. A., Seidner, A. L., Robbins-Sisco, D., Krinsky, A., & Hanser, S. B. (1992). Batter up! Relapse prevention for homeless veteran substance abusers via softball team participation. *Journal of Substance Abuse*, 4(4), 407-413.
- Callaghan, P. (2004). Exercise: a neglected intervention in mental health care? *Journal of Psychiatric and Mental Health Nursing*, 11(4), 476-483. doi: 10.1111/j.1365-2850.2004.00751.
- Caspersen, C.J., Powell, K.E., Christenson, G.M. (1985) Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Report*. 100(2): 126–131.
- Cohen, J. (1977). *Statistical Power Analysis for the Behavioral Sciences (Revised Edition)*. Mahwah: Lawrence Erlbaum Associates.
- Cohen, S., Kamarck, T., & Mermelstein, R. (1983). A Global Measure of Perceived Stress. *Journal of Health and Social Behaviour*, 24, 385-396.
- Collingwood, T. R., Reynolds, R., Kohl, H. W., Smith, W., & Sloan, S. (1991). Physical fitness effects on substance abuse risk factors and use patterns. *Journal of Drug Education*, 21(1), 73-84.

- Cooney, G. M., Dwan, K., Greig, C. A., Lawlor, D. A., Rimer, J., Waugh, F. R., McMurdo, M., Mead, G. E. (2013). Exercise for depression. *Cochrane Database Systematic Reviews*, 9, CD004366. doi: 10.1002/14651858.CD004366.pub6
- Craig, C. L., Marshall, A. L., Sjoström, M., Bauman, A. E., Booth, M. L., Ainsworth, B. E., Pratt, M., Ekelund, U., Yngve, A., Sallis, J.F., Oja, P. (2003). International physical activity questionnaire: 12-country reliability and validity. *Medicine & Science in Sports & Exercise*, 35(8), 1381-1395. doi: 10.1249/01.mss.0000078924.61453.fb
- Cutter, C. J., Schottenfeld, R. S., Moore, B. A., Ball, S. A., Beitel, M., Savant, J. D., Stults-Kolehmainen, M. A., Doucette, C., Barry, D. T. (2014). A pilot trial of a videogame-based exercise program for methadone maintained patients. *Journal of Substance Abuse Treatment*, 47(4): 299–305. doi: <http://dx.doi.org/10.1016/j.jsat.2014.05.007>
- Dart, R. C., Surratt, H. L., Cicero, T. J., Parrino, M. W., Severtson, S. G., Bucher-Bartelson, B., & Green, J. L. (2015). Trends in Opioid Analgesic Abuse and Mortality in the United States. *New England Journal of Medicine*, 372(3), 241-248. doi: doi:10.1056/NEJMs1406143
- Dolezal, B. A., Chudzynski, J., Dickerson, D., Mooney, L., Rawson, R. A., Garfinkel, A., & Cooper, C. B. (2014). Exercise training improves heart rate variability after methamphetamine dependency. *Medicine & Science in Sports & Exercise*, 46(6), 1057-1066. doi: 10.1249/mss.0000000000000201
- Dolezal, B. A., Chudzynski, J., Storer, T. W., Abrazado, M., Penate, J., Mooney, L., Dickerson, D., Rawson, R. A., Cooper, C. B. (2013). Eight weeks of exercise training improves fitness measures in methamphetamine-dependent individuals in residential treatment. *Journal of Addiction Medicine*, 7(2), 122-128. doi: 10.1097/ADM.0b013e318282475e
- Fischer, B., Oviedo-Joekes, E., Blanken, P., Haasen, C., Rehm, J., Schechter, M. T., Strang, J., van den Brink, W. (2007). Heroin-assisted treatment (HAT) a decade later: a brief update on science and politics. *Journal of Urban Health*, 84(4), 552-562. doi: 10.1007/s11524-007-9198-y

- Gebel, K., Ding, D., Chey, T., Stamatakis, E., Brown, W. J., & Bauman, A. E. (2015). Effect of Moderate to Vigorous Physical Activity on All-Cause Mortality in Middle-aged and Older Australians. *JAMA Internal Medicine*, 175(6), 970-977. doi: 10.1001/jamainternmed.2015.0541
- Hautzinger, M., & Bailer, M. (1993). Allgemeine Depressions-Skala. Beltz, Weinheim.
- Hawkins, M. N., Raven, P. B., Snell, P. G., Stray-Gundersen, J., & Levine, B. D. (2007). Maximal oxygen uptake as a parametric measure of cardiorespiratory capacity. *Medicine & Science in Sports & Exercise*, 39(3), 574-574. doi: 10.1097/mss.0b013e31803d3c55
- Hiltebrand, D., Dickson-Spillmann, M., Bolliger, H., & Schaub, M. (2015). *Heroingestützte Behandlung in der Schweiz. Resultate der Erhebung 2014*. Zürich: Swiss Research Institute for Public Health and Addiction.
- Hjorthøj, C. R., Hjorthøj, A. R., & Nordentoft, M. (2012). Validity of Timeline Follow-Back for self-reported use of cannabis and other illicit substances — Systematic review and meta-analysis. *Addictive Behaviors*, 37(3), 225-233. doi: <http://dx.doi.org/10.1016/j.addbeh.2011.11.025>
- Hupin, D., Roche, F., Gremeaux, V., Chatard, J.-C., Oriol, M., Gaspoz, J.-M., Barthelemy, J.C., Edouard, P. (2015). Even a low-dose of moderate-to-vigorous physical activity reduces mortality by 22% in adults aged ≥60 years: a systematic review and meta-analysis. *British Journal of Sports Medicine*. doi: 10.1136/bjsports-2014-094306
- Kleber, H.D., Weiss, R. D., Anton, R. F., George, T. P., Greenfield, S. F., Kosten, T. R., O'Brien, C. P., Rounsaville, B. J., Strain, E. C., Ziedonia, D. M., Hennessey, G., Smith Connery, H. (2006) *Practice Guideline for the treatment of Patients With Substance Use Disorders* (2nd. Ed) Arlington: American Psychiatric Association.
- Lee, P. H., Macfarlane, D. J., Lam, T. H., & Stewart, S. M. (2011). Validity of the International Physical Activity Questionnaire Short Form (IPAQ-SF): a systematic review. *International Journal of Behavioral Nutrition and Physical Activity*, 8, 115. doi: 10.1186/1479-5868-8-115

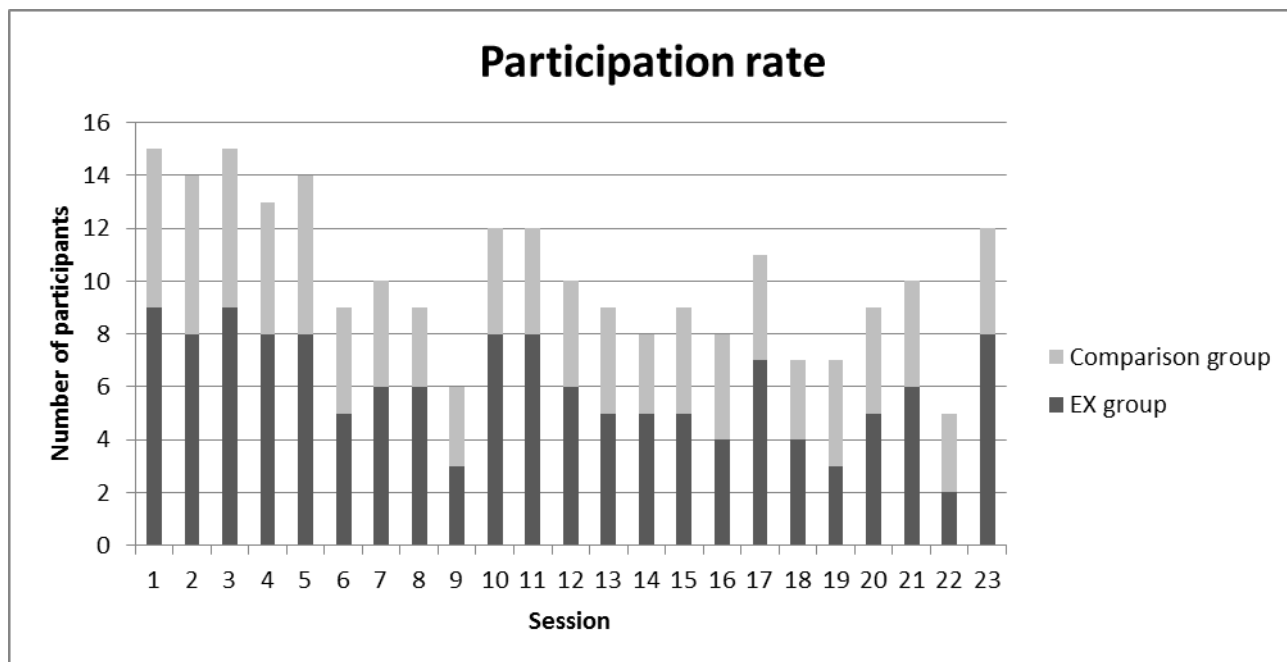
- Lehr, D., Hillert, A., Schmitz, E., & Sosnowsky, N. (2008). Screening depressiver Störungen mittels Allgemeiner Depressions-Skala (ADS-K) und State-Trait Depressions Scales (STDS-T). *Diagnostica*, 54(2), 61-70. doi: doi:10.1026/0012-1924.54.2.61
- Li, M., Chen, K., & Mo, Z. (2002). Use of qigong therapy in the detoxification of heroin addicts. *Alternative Therapy in Health and Medicine*, 8(1), 50-54, 56-59.
- Linke, S. E., & Ussher, M. (2015). Exercise-based treatments for substance use disorders: evidence, theory, and practicality. *American Journal of Drug and Alcohol Abuse*, 41(1), 7-15. doi: 10.3109/00952990.2014.976708
- Lynch, W. J., Peterson, A. B., Sanchez, V., Abel, J., & Smith, M. A. (2013). Exercise as a novel treatment for drug addiction: A neurobiological and stage-dependent hypothesis. *Neuroscience & Biobehavioral Reviews*, 37(8), 1622-1644. doi: 10.1016/j.neubiorev.2013.06.011
- Maloney, P. W., Grawitch, M. J., & Barber, L. K. (2012). The multi-factor structure of the Brief Self-Control Scale: Discriminant validity of restraint and impulsivity. *Journal of Research in Personality*, 46(1), 111-115. doi: <http://dx.doi.org/10.1016/j.jrp.2011.10.001>
- Mooney, L. J., Cooper, C., London, E. D., Chudzynski, J., Dolezal, B., Dickerson, D., Brecht, M.L., Penate, J., Rawson, R. A. (2014). Exercise for methamphetamine dependence: Rationale, design, and methodology. *Contemporary Clinical Trials*, 37(1), 139-147. doi: <http://dx.doi.org/10.1016/j.cct.2013.11.010>
- Morin, C. M., Belleville, G., Belanger, L., & Ivers, H. (2011). The Insomnia Severity Index: Psychometric Indicators to Detect Insomnia Cases and Evaluate Treatment Response. *Sleep*, 34(5), 601-608.
- Nutt, D.J., Lingford-Highes, A., Erritzoe, D., Stokes, P. R. (2015) The dopamine theory of addiction: 40 years of highs and lows. *National Review of Neuroscience*, 16(5):305-12. doi: 10.1038/nrn3939.

- Pattyn, N., Cornelissen, V. A., Eshghi, S. R., & Vanhees, L. (2013). The effect of exercise on the cardiovascular risk factors constituting the metabolic syndrome: a meta-analysis of controlled trials. *Sports Medicine*, 43(2), 121-133. doi: 10.1007/s40279-012-0003-z
- Pickering, T. G., Hall, J. E., Appel, L. J., Falkner, B. E., Graves, J., Hill, M. N., Jones, D. W., Kurtz, T., Sheps, S. G., Roccella, E. J. (2005). Recommendations for Blood Pressure Measurement in Humans and Experimental Animals: Part 1: Blood Pressure Measurement in Humans: A Statement for Professionals From the Subcommittee of Professional and Public Education of the American Heart Association Council on High Blood Pressure Research. *Circulation*, 111(5), 697-716. doi: 10.1161/01.cir.0000154900.76284.f6
- Richardson, C. R., Faulkner, G., McDevitt, J., Skrinar, G. S., Hutchinson, D. S., & Piette, J. D. (2005). Integrating physical activity into mental health services for persons with serious mental illness. *Psychiatric Services*, 56(3), 324-331. doi: 10.1176/appi.ps.56.3.324
- Roberti, J. W., Harrington, L. N., & Storch, E. A. (2006). Further Psychometric Support for the 10-Item Version of the Perceived Stress Scale. *Journal of College Counseling*, 9(2), 135-147. doi: 10.1002/j.2161-1882.2006.tb00100.x
- Robertson, C. L., Ishibashi, K., Chudzynski, J., Mooney, L. J., Rawson, R. A., Dolezal, B. A., Cooper, C. B., Brown, A. K., Mandelkern, M. A., London, E. D. (2015). Effect of Exercise Training on Striatal Dopamine D2/D3 Receptors in Methamphetamine Users during Behavioral Treatment. *Neuropsychopharmacology*, 41(6):1629-36doi: 10.1038/npp.2015.331
- Roessler, K. K. (2010). Exercise treatment for drug abuse--a Danish pilot study. *Scandinavian Journal of Public Health*, 38(6), 664-669. doi: 10.1177/1403494810371249
- Rosenbaum, S., Tiedemann, A., Sherrington, C., Curtis, J., & Ward, P. B. (2014). Physical activity interventions for people with mental illness: a systematic review and meta-analysis. *Journal of Clinical Psychiatry*, 75(9), 964-974. doi: 10.4088/JCP.13r08765
- Sasaki, H., Kasagi, F., Yamada, M., Fujita, S. (2007). Grip strength predicts cause-specific mortality in middle-aged and elderly persons. *American Journal of Medicine*. 120(4), 337-342

- Sobell, L. C., Maisto, S. A., Sobell, M. B., & Cooper, A. M. (1979). Reliability of alcohol abusers' self-reports of drinking behavior. *Behaviour Research and Therapy*, 17(2), 157-160.
- Sobell, L. C., & Sobell, M. B. (1996). *Timeline followback: A calendar method for assessing alcohol and drug use*. Paper presented at the Addiction Research Foundation.
- Tangney, J. P., Baumeister, R. F., & Boone, A. L. (2004). High self-control predicts good adjustment, less pathology, better grades, and interpersonal success. *Journal of Personality*, 72(2), 271-324.
- Taylor, R. S., Brown, A., Ebrahim, S., Jolliffe, J., Noorani, H., Rees, K., Skidmore, B., Stone, J. A., Thompson, D. R., Oldridge, N. (2004). Exercise-based rehabilitation for patients with coronary heart disease: systematic review and meta-analysis of randomized controlled trials. *The American Journal of Medicine*, 116(10), 682-692. doi: <http://dx.doi.org/10.1016/j.amjmed.2004.01.009>
- Trivedi, M. H., Greer, T. L., Grannemann, B. D., Church, T. S., Somoza, E., Blair, S. N., Szapocznik, J., Stoutenberg, M., Rethorst, C., Warden, D., Ring, K. M., Walker, R., Morris, D.W., Kosinski, A.S., Kyle, T., Marcus, B., Crowell, B., Oden, N., Nunes, E. (2011). Stimulant reduction intervention using dosed exercise (STRIDE) - CTN 0037: study protocol for a randomized controlled trial. *Trials*, 12, 206. doi: 10.1186/1745-6215-12-206
- van Poppel, M. N., Chinapaw, M. J., Mokkink, L. B., van Mechelen, W., & Terwee, C. B. (2010). Physical activity questionnaires for adults: a systematic review of measurement properties. *Sports Medicine*, 40(7), 565-600. doi: 10.2165/11531930-000000000-00000
- Volkow, N. D. (2001). Drug Abuse and Mental Illness: Progress in Understanding Comorbidity. *American Journal of Psychiatry*, 158(8), 1181-1183. doi: doi:10.1176/appi.ajp.158.8.1181
- Weiss, L., Gass, J., Egan, J. E., Ompad, D. C., Trezza, C., & Vlahov, D. (2014). Understanding Prolonged Cessation from Heroin Use: Findings from a Community-Based Sample. *Journal of Psychoactive Drugs*, 46(2), 123-132. doi: 10.1080/02791072.2014.890765

- Williams, D. M. (2008). Exercise, affect, and adherence: an integrated model and a case for self-paced exercise. *Journal of Sport, Exercise & Psychology*, 30(5), 471-496.
- Zschucke, E., Heinz, A., & Strohle, A. (2012). Exercise and physical activity in the therapy of substance use disorders. *ScientificWorldJournal*, 2012, 901741. doi: 10.1100/2012/901741
- Zschucke, E., Gaudlitz, K., & Ströhle, A. (2013). Exercise and Physical Activity in Mental Disorders: Clinical and Experimental Evidence. *Journal of Preventive Medicine and Public Health*, 46(Suppl 1), S12-S21. doi: 10.3961/jpmph.2013.46.S.S12

Figure 1. Participant numbers for each of the 23 intervention sessions, separately for exercise condition and comparison condition



Note: N=24(EX : n=13 ; Comparison: n=11). EX: exercise conditio

Table 1.Descriptive and Inferential Statistics for Demographic Variables, separately for exercise condition and control condition

	EX (n=13)	Control (n=11)		
	M (SD)	M (SD)	F	p
Age (Years)	42.7(6.5)	45.8(4.2)	1.73	.201
Diacetylmorphine dose per day (mg)	377 (164)	400 (162)	.066	.802
	N (%)	N (%)	χ^2	p
Women	4 (30.8)	5 (37.5)	.548	.459
Men	9 (69.2)	6 (62.5)		
Employed	4(30.8)	1(9.1)	1.968	.193
Unemployed	9(69.2)	10(90.9)		
Education beyond high school	8(61.5)	6(54.5)	.120	.729
No education beyond high school	5(38.5)	5(45.5)		
Single	8(61.5)	9(81.8)	1.570	.456
Married	1(7.7)	0(0.0)		
Divorced	4(30.8)	2(18.2)		
Psychiatric comorbidity diagnosed	6(46.2)	6(54.5)	.168	.682
No psychiatric comorbidity diagnosed	7(53.8)	5(45.5)		

Note: N=24. EX= Exercise condition

Table 2. Descriptive and Inferential Statistics for Compliance rates, separately for exercise and control conditions

	EX (n=13)	Control (n=11)		
	N (%)	N (%)	χ^2	p
Compliant	5 (38.5)	5 (45.5)	7.049	.029
Semi-Compliant	7 (53.8)	1 (9.1)		
Non-Compliant	1 (7.7)	5 (45.5)		

Note: N=24. EX= Exercise condition. Compliant: Missed fewer than 5 of 23 sessions. Semi-Compliant: Missed between 6 and 18 of 23 sessions. Non-Compliant: Missed 19 or more of 23 sessions.

Table 3. Descriptive and Inferential statistics for Depression, Subjective Sleep, Self-Control, Perceived Stress, and Quality of Life, separately for exercise condition and control condition.

	Group	Baseline M (SD)	6 Weeks M (SD)	12 Weeks M (SD)	F (P Value) η^2 Time effect	F (P Value) η^2 Group Effect	F (P Value) η^2 Interaction effect
ADS	EX	15.23(11.42)	13.31(9.74)	13.54(10.83)	.930(.403) .044	.452(.509) .022	.301(.742) .015
	Control	17.44(6.78)	17.11(6.25)	15.11(9.07)			
ISI	EX	12.00(7.52)	11.85(8.255)	11.08(7.66)	2.371(.106) .106	1.380(.254) .065	.636(.535) .031
	Control	9.67(5.45)	8.00(5.172)	7.33(3.77)			
BSC	EX	38.85(6.90)	40.46(8.35)	40.85(6.42)	1.546(.230) .072	.603(.447) .029	2.760(.093) .121
	Control	39.22(8.72)	35.00(7.17)	39.00(8.44)			
PSS	EX	16.92(8.09)	17.31(7.67)	17.15(7.35)	.071(.931) .004	.452(.509) .025	.157(.855) .008
	Control	19.33(6.25)	18.89(7.11)	19.67(6.80)			
SF36 - 1	EX	95.77(5.34)	86.92(13.31)	91.92(8.04)	1.609(.213) .074	6.951(.016) .258	.564(.574) .027
	Control	77.78(16.97)	75.56(22.14)	77.78(23.33)			
SF36 - 2	EX	75.00(22.82)	73.08(43.85)	59.62(43.94)	.332(.720) .016	1.343(.260) .063	1.307(.282) .061
	Control	44.44(37.03)	58.33(41.45)	58.33(43.30)			
SF36 - 4	EX	60.23(24.91)	64.92(22.34)	60.92(25.80)	.386(.681) .019	.604(.446) .029	.492(.615) .024
	Control	54.11(14.69)	55.22(13.70)	58.22(9.74)			
SF36- 5	EX	50.00(20.20)	45.77(14.97)	46.54(18.75)	.376(.689) .018	1.208(.285) .057	.416(.663) .020
	Control	40.56(13.33)	41.67(16.00)	38.89(14.53)			
SF36- 6	EX	71.15(27.18)	79.81(25.78)	76.92(20.31)	1.563(.222) .073	.990(.332) .047	1.018(.370) .048
	Control	66.67(24.20)	69.44(20.83)	62.50(27.24)			
SF36- 7	EX	53.85(37.36)	64.10(37.172)	64.15(37.20)	1.984(.151) .090	3.408(.080) .146	1.101(.343) .052
	Control	29.63(45.47)	44.45(37.26)	25.93(36.46)			
SF36- 8	EX	60.92(20.85)	60.92(25.72)	64.92(24.88)	.676(.514) .033	.572(.458) .028	.596(.556) .029
	Control	53.33(18.54)	57.33(19.07)	55.56(19.53)			

Note: N=24(EX : n=13 ; Control: n=11). EX: exercise condition. ADS: Allgemeine Depressionsskala – Kurz. ISI: Insomnia Severity Index. BSC: Brief Self Control Scale. PSS: Perceived Stress Scale. SF36 1-8: Short Form Health Survey Questionnaire

Table 4. Descriptive and Inferential Statistics for Secondary Substance Consumption, separately for exercise condition and control condition.

	Group	Baseline M(SD)	6 weeks M(SD)	12 weeks M(SD)	F (P Value) η^2 Time effect	F (P Value) η^2 Group Effect	F (P Value) η^2 Interaction effect
Days secondary drug consumption	EX	8.92(8.91)	9.85(9.92)	7.85(9.91)	.672(.516) .031	.655(.427) .030	1.631(.208) .072
	Control	14.60(13.77)	9.50(12.89)	12.90(13.32)			
Days illicit heroin consumption	EX	.23(.59)	.31(.85)	.46(1.19)	.013(.953) .001	1.001(.328) .046	.828(.402) .038
	Control	.20(.42)	.10(.31)	.00(.00)			
Days illicit cocaine consumption	EX	1.38(2.21)	3.08(7.63)	.38(1.12)	.888(.362) .041	.309(.584) .015	1.158(.297) .052
	Control	3.00(8.80)	3.00(8.80)	3.20(8.74)			
Days alcohol consumption	EX	7.08(8.86)	5.92(8.60)	7.69(10.01)	2.125(.132) .092	.962(.338) .044	.701(.502) .032
	Control	5.90(8.60)	.90(1.66)	4.50(8.78)			
Days cigarette consumption	EX	27.38(2.21)	28.00(.00)	28.00(.00)	.741(.483) .034	1.023(.323) .046	1.811(.176) .079
	Control	28.00(.00)	25.20(8.85)	25.20(8.85)			
Days unprescribed medication consumption	EX	1.46(2.60)	.38(1.38)	.08(.277)	2.204(.138) .095	2.043(.168) .089	2.204(.095) .095
	Control	.10(.316)	.10(.316)	.10(.316)			

Note: N=24 (EX : n=13 ; Control: n=11). EX: exercise condition.

Table 5. Descriptive and Inferential statistics for Self-reported activity and physiological measures, separately for exercise and control conditions.

	Group	Baseline M(SD)	6 Weeks M(SD)	12 Weeks M(SD)	F (P Value) η^2 Time effect	F (P Value) η^2 Group Effect	F (P Value) η^2 Interaction effect
IPAQ – 1	EX	1.15(1.46)	1.92(1.70)	4.08(8.79)	.628(.451) .030	1.050(.318) .050	.989(.339) .047
	Control	1.11(1.61)	1.44(2.65)	.89(1.69)			
IPAQ – 2	EX	23.08(27.12)	41.54(39.28)	36.92(29.12)	.293(.682) .014	.870(.362) .042	3.794(.046) .159
	Control	28.33(34.73)	15.00(27.04)	23.33(36.82)			
IPAQ – 3	EX	2.54(2.78)	3.92(3.22)	3.00(2.30)	1.345(.272) .063	2.133 (.160) .096	.766(.472) .037
	Control	2.22(2.38)	2.33(2.82)	1.22(1.09)			
IPAQ – 4	EX	68.08(97.33)	75.00(90.83)	41.54(31.31)	.505(.607) .025	1.721(.204) .096	.773(.468) .037
	Control	35.00(34.36)	30.00(35.17)	35.00(35.96)			
IPAQ – 5	EX	6.08(2.29)	6.38(1.44)	5.08(2.53)	2.758(.101) .121	.378(.546) .019	.103(.903) .005
	Control	5.44(2.60)	5.67(2.69)	4.78(3.15)			
IPAQ - 6	EX	71.54(56.84)	84.23(68.06)	68.08(59.56)	.377(.629) .018	3.404(.080) .145	.434(.595) .021
	Control	41.67(20.91)	40.00(16.77)	40.00(23.71)			
Systolic pressure	EX	131.67(16.79)	129.76(18.89)	130.48(18.57)	1.145(.329) .054	.007(.963) .000	1.152(.326)
	Control	133.00(13.63)	134.27(17.09)	126.31(18.78)			
Diastolic pressure	EX	85.30(9.24)	82.46(10.70)	84.87(14.32)	.962(.391) .046	.105(.750) .005	.013(.987) .001
	Control	87.11(9.05)	83.53(13.10)	86.09(12.77)			
Handgrip right	EX	45.53(12.34)	43.25(10.63)	44.38(9.12)	.101(.849) .005	5.558(.029) .217	1.550(.229) .072
	Control	32.66(10.56)	36.48(11.22)	34.33(10.09)			
Handgrip left	EX	42.94(10.69)	41.38(8.92)	43.64(7.20)	.827(.397) .040	8.709(.008) .303	.179(.730) .009
	Control	31.74(9.16)	31.25(9.19)	32.11(9.61)			

Note: N=24(EX : n=13 ; Control: n=11).. EX: exercise condition. IPAQ1-6: International Physical Activity Questionnaire